Rejections Under 35 U.S.C. § 112, First Paragraph

The Examiner rejected claims 1, 2, 5, 7, 9, 11, 14 and 76-83 under 35 U.S.C. § 112, first paragraph for lack of an adequate written description. Although Applicants believe that the rejection is not supported by the case law cited by the Examiner (which cases pertain to unknown gene sequences and not fragments of a known protein), the claim amendments made herewith are believed to obviate the rejection. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection made under 35 U.S.C 112, first paragraph.

Rejections Under 35 U.S.C. § 102

The Examiner rejected claims 1, 2, 7, 11, 76, and 80-82 under 35 U.S.C. § 102(b) as anticipated by the Fikes PCT application (WO95/04542). Applicants have canceled claim 1 and amended claim 2 to further define the amino acid sequence of the HLA class II binding peptide. Claim 11 has been canceled. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection made under 35 U.S.C. § 102(b).

The Examiner rejected claims 1, 2, 9, 11 and 80 under 35 U.S.C. § 102(b) as anticipated by the Topalian PCT application (WO97/11669).

The sections of the Topalian PCT application cited by the Examiner relate to a method for screening melanoma antigens for the presence of HLA class II tumor associated antigens, including the MAGE-1 melanoma antigen. There is nothing in this reference that shows that MAGE-1 actually contains a class II antigen. Topalian et al. have merely made the suggestion that MAGE-1 could contain a class II antigen, and have accordingly claimed a method for finding such putative antigens.

The amendments to the claims obviate the rejection based on Topalian, because Topalian does not identify which portion of MAGE-1 might contain a HLA class II binding peptide. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection made under 35 U.S.C. § 102(b).

The Examiner rejected claims 1 and 2 under 35 U.S.C. § 102(e) as anticipated by the Chaux et al. reference.

The Chaux paper recites HLA class II binding peptides of a different MAGE protein, MAGE-A3. Because the claim amendment proposed above restricts the MAGE-A1 HLA class II binding peptide sequence to SEQ ID NO:7 with one possible amino acid substitution and 0-10 amino acid additions at either or both ends, the peptides provided in the Chaux reference do not anticipate the claimed invention. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection made under 35 U.S.C. § 102(e).

The Examiner rejected claims 1, 2, 5, 7, 9, 11, 14, 78-80 and 83 under 35 U.S.C. § 102(a) as anticipated by the Thielemans PCT application (WO99/14326).

The Thielemans application discloses MAGE-A3 HLA class II binding peptides and their uses. The Thielemans application does not disclose fragments of MAGE-A1 as HLA class II binding peptides, particularly as now claimed. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection made under 35 U.S.C. § 102(a).

The Examiner rejected claims 1, 2, 5, 7, 78 and 79 under 35 U.S.C. § 102(e) as anticipated by the Chaux patent (US 5,965,535).

The Examiner stated that Chaux teaches certain features of the claimed invention, but also stated that "Thielemans" teaches D-amino acids and conjugation to MAGE-1 class I binding peptides. Applicants have assumed for the purpose of this response that the Examiner meant to refer to Chaux throughout this portion of the rejection.

Chaux discloses MAGE-A3 HLA class II binding peptides and their uses, but does not disclose fragments of MAGE-A1 as HLA class II binding peptides. In view of the claim amendments, Applicants believe that none of the claims are anticipated by the Chaux patent. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection made under 35 U.S.C. § 102(e).

Rejections Under 35 U.S.C. § 103

The Examiner rejected claims 1, 2, 9, 11, 76, 77, 80-82 under 35 U.S.C. § 103 as unpatentable over WO95/04542 (Fikes et al.).

The Examiner has based this rejection on the teaching of a peptide in claim 3 of the Fikes PCT application. Claim 3 listed a peptide that consists of 9 of the 12 amino acids of SEQ ID

NO:7 of the instant application. The Fikes peptide is designated SEQ ID NO:8 (YVIKVSARV), and is claimed as a HLA-A2 binding peptide. SEQ ID NO:8 of Fikes is missing the first amino acid (E) and the last two amino acids (R, F) of SEQ ID NO:7 of the present application. The Examiner reasons that one of ordinary skill in the art would have been motivated to add the missing amino acids to SEQ ID NO:8 of Fikes to make SEQ ID NO:7 because Fikes taught that amino acids could be added to either or both ends.

Based on the amendments to the claims, this rejection should not stand. First, Fikes did not teach that amino acids should be added, merely that they can be added. Given that Fikes taught that SEQ ID NO:8 was an immunogenic peptide (in claim 3), one of ordinary skill in the art would not be motivated to add any amino acids to both ends. Moreover, there certainly was not any motivation to add the correct number of amino acids to the correct ends of SEQ ID NO:8. Further, there was no suggestion by Fikes to add the specific amino acids contained in SEQ ID NO:7, and thus one of ordinary skill in the art would not have been motivated to do so. There is no specific and clear motivation in the references cited by the Examiner or in the general knowledge of one of ordinary skill in the art to make the specific number and kind of substitutions that would be required to arrive at the sequence of SEQ ID NO:7 starting with the SEQ ID NO:8 peptide of Fikes.

Therefore, Applicants respectfully request that the Examiner withdraw the rejection of the claims under 35 U.S.C. § 103 based on WO95/04542 (Fikes et al.).

The Examiner rejected claims 5, 14, 78 and 83 under 35 U.S.C. § 103 as unpatentable over Fikes et al. (WO95/04542) in combination with Sanderson et al.

This rejection is similar to the previous Fikes obviousness rejection with the addition of the Sanderson reference to teach the Ii invariant chain for targeted fusions. As above, one of ordinary skill in the art would not have been motivated to add the correct number and kind of amino acids to arrive at the claimed peptides. Sanderson does not cure the essential deficiency of Fikes.

Accordingly, Applicants respectfully request that the Examiner withdraw the rejection of the claims under 35 U.S.C. § 103 based on WO95/04542 (Fikes et al.) in combination with Sanderson et al.

The Examiner rejected claims 1, 2, 5, 9, 11, 14, 78, 80 and 83 under 35 U.S.C. § 103 as unpatentable over WO97/11669 (Topalian et al.) in combination with Sanderson et al.

This rejection is based on the combination of Topalian (for functional variants of SEQ ID NO:7) and Sanderson (for Ii). Based on the claim amendments and arguments set forth above for the Topalian anticipation rejection, Applicants respectfully request that the Examiner withdraw this rejection of the claims under 35 U.S.C. § 103.

The Examiner rejected claims 7 and 79 under 35 U.S.C. § 103 as unpatentable over WO95/04542 (Fikes et al.) in view of US patent 6,043,347 (Gelder et al.). The Examiner also rejected claims 1, 2, 5, 9, 11, 14, 78, 80 and 83 over WO97/11669 (Topalian et al.) in view of US patent 6,043,347 (Gelder et al.).

These rejections are based on the previous Fikes or Topalian obviousness rejections with the addition of the Gelder reference to teach D-amino acids. Based on the claim amendments and arguments set forth above for the respective Fikes and Topalian rejections, Applicants respectfully request that the Examiner withdraw this rejection of the claims under 35 U.S.C. § 103.

In view of the amendments and the arguments presented above, Applicants respectfully request that the rejections of the claims be withdrawn. If the Examiner wishes to expedite the prosecution of this application in any way, then the Examiner is invited to contact the Applicants' representative at the telephone number listed below.

Respectfully submitted,

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Amended Claims

2.(amended) An [The] isolated HLA class II-binding peptide [of claim 1 wherein the isolated peptide comprises] consisting essentially of

the amino acid sequence set forth as SEQ ID NO:7, or a functional variant thereof comprising one amino acid addition, substitution or deletion, and

0-10 amino acids added to either or both ends of the amino acid sequence set forth as SEQ ID NO:7, or the functional variant thereof.

5.(amended) The isolated HLA class II-binding peptide of claim [1] 2 wherein the isolated peptide comprises an endosomal targeting signal.

7.(amended) The isolated HLA class II-binding peptide of claim [1] 2 wherein the isolated peptide is non-hydrolyzable.

9.(amended) A composition comprising an isolated MAGE-A1 HLA class I-binding peptide and an isolated MAGE-A1 HLA class II-binding peptide, wherein the isolated HLA class II-binding peptide consists essentially of

the amino acid sequence set forth as SEQ ID NO:7, or a functional variant thereof comprising one amino acid addition, substitution or deletion, and

0-10 amino acids added to either or both ends of the amino acid sequence set forth as SEQ ID NO:7, or the functional variant thereof.

76.(amended) The isolated HLA class II-binding peptide of claim 2 wherein the isolated peptide [comprises] consists essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4, and SEQ ID NO:7.

81.(amended) The composition of claim [11] 9 wherein the isolated MAGE-A1 HLA class II-binding peptide [comprises] consists essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

82.(amended) The composition of claim [11] 9 wherein the isolated MAGE-A1 HLA class II-binding peptide consists of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.